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EXAMINER
GRASER, JENNIFER E

ART UNIT	PAPER NUMBER
1645	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/844,281	Applicant(s) Mangold et al.
	Examiner Jennifer Graser	Art Unit 1645

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Election 5/29/03*

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-43* is/are pending in the application.

4a) Of the above, claim(s) *1-15 and 21-43* is/are withdrawn from consideratio

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *16-20* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☐ Notice of References Cited (PTO-892)

16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). *8 & 12*

18) ☐ Interview Summary (PTO-413) Paper No(s). _____

19) ☐ Notice of Informal Patent Application (PTO-152)

20) ☐ Other:

DETAILED ACTION

Election/Restriction

1. Applicant's election with traverse of Group II, claims 16-20, in Paper No. 11 is acknowledged. The traversal is on the ground(s) that it would not place a serious burden on the Examiner to examine all of the groups together. Applicants argue that since all of the claims are directed to tools and methods for immunological detection of anthrax there would be no serious burden on the Examiner. Applicants go on to argue that an examination of 3 Classes is not a burden. This is not found persuasive because, as outlined in the former Restriction Requirement, place an undue burden on the Examiner to examine all of these different inventions together. Class 435, 530 and 435 are extremely large Classes with over 900 subclasses within them. Even a search of a single subclass contains thousands of patents. With respect to the other groups, as stated in the former Restriction Requirement,:

Inventions I and VIII are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case, the antibodies of Group I may be used in methods other than passive immunization, i.e., they may be used in detection methods. Inventions I and III are related as process of making and product made. The inventions are distinct if either or both of the following can be shown: (1) that the process as claimed can be used to make other and materially different product or (2) that the product as claimed can be made by another and materially different process (MPEP § 806.05(f)). In the instant case, the antibodies of Group I may be made by a different method than that described in Group III, i.e., the antibodies may be synthetically produced. Inventions VI and VII are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP

§ 806.05(h)). In the instant case, the protein of Group VI may be used in methods other than detection, i.e., it may be used as an immunogen.

The requirement is still deemed proper and is therefore made **FINAL**. Claims 1-15 and 21-43 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 16-20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 16 is indefinite because it fails to clarify that the antibody is "isolated", i.e, not a product of nature. Additionally, it is preferred that "specifically reactive" be changed to "specifically binds".

Claim 16 is vague and confusing because it appears to fail to claim what Applicant regards as the invention. A review of the specification teaches that Applicants intend to claim antibodies which specifically bind to *B.anthracis* and do not cross-react with other species of *Bacillus*. More particularly, it appears that isolated antibodies which bind to the EA1 antigen appear to be the inventive concept. However, claim 16 is drawn to antibodies which can bind any one of *B.anthracis, B.thuingiensis,* or *B.cereus*. Clarification is requested.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claim 20 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Enablement requires that the specification teach those in the art to make and use the invention without undue experimentation. Factors to be considered in determining whether a disclosure would require undue experimentation include (1) the nature of the invention, (2) the state of the prior art, (3) the predictability or lack thereof in the art, (4) the amount of direction or guidance present, (5) the presence or absence of working examples, (6) the quantity of experimentation necessary, (7) the relative skill of those in the art, and (8) the breadth of the claims.

Claim 20 is drawn to a diagnostic kit which comprises an antibody that is specifically reactive against spores of *B.thuringiensis* and not *B.anthracis*. However, the instant specifcation is only enabled for antibodies which are specific to *B.anthracis*. The specification fails to identify any epitopes unique to antigens of *B.thuringiensis*. A prophetic method for developing antibodies specific to *Bacillus* species other than *B.anthracis* is described briefly on pages 6-7, yet no examples are provided. Additionally, no unique antigens or their epitopes from

B.thuringiensis are identified. It would take undue experimentation for one of skill in the art to identify a completely new unique antibody which displays no cross-reactivity to other members of its Genus. The specification has only enabled antibodies unique to *B.anthracis*. There is a great deal of unpredictability in finding antibodies which can distinguish between the different species of *Bacillus*. There is very little guidance provided in the specification for finding an antibody unique to *B.thuringiensis* with no cross-reactivity to other species of Bacillus. There are no working examples provided with respect to *B.thuringiensis* antibodies. While the skill of those in the art is high, the quantity of experimentation would be undue given the limited guidance provided by the specifcation. Lastly, the title of the invention is "Anthrax Specific Antibodies".

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 16-19 are rejected under 35 U.S.C. 102(a) as being anticipated by Long et al (J.Applied Microbio., August 1999. 87:214).

Long et al teach an antibody-based system for the detection of *Bacillus anthracis* in environmental samples. The reference teaches that they have developed antigen capture dipstick

assays which can detect antibodies to *B.anthracis* protective antigen and also dipsticks which can detect antibodies for *B.anthracis* spores. It is taught that colloidal gold is used to visualize the reaction. This is colloidal particle based lateral flow detection system. Although the reference does not specifically recite that the assay is not reactive against spores of *B.thuringiensis,* it does recite that the assay is specific for the detection and identification of *B.anthracis.* The kit of claims 16-19 only requires antibody and a colloidal particle based lateral flow detection system and is therefore clearly anticipated by Long et al.

8. Claim 16 is rejected under 35 U.S.C. 102(b) as being anticipated by Mesnage et al (Molec. Microbiol. 1997, 23(6): 1147-1155).

Mesnage et al teach antibodies to the *Bacillus anthracis* S-layer component, EA1. Antibodies to the surface array protein (Sap) are also taught. The kit of claim 16 only requires antibody to a spore *or* vegetative cell of any one of *Bacillus anthracis, B.thuringiensis* or *B.cereus* and is therefore anticipated by the reference.

9. Claim 16 is rejected under 35 U.S.C. 102(b) as being anticipated by Phillips et al (FEMS Microbio. Immunol. 1988. 47: 169-178).

Phillips et al teach monoclonal antibodies against spore antigens of *Bacillus anthracis.* The kit of claim 16 only requires antibody to a spore *or* vegetative cell of any one of *Bacillus anthracis, B.thuringiensis* or *B.cereus* and is therefore anticipated by the reference.

10. Claim 16 is rejected under 35 U.S.C. 102(b) as being anticipated by Wright et al (WO 86/02363).

Wright et al teach monoclonal antibodies against antigens of *Bacillus,* including *B.cereus* and *B.anthracis*. Kits comprising the antibodies are specifically taught. See page 13 and claim 38. The kit of claim 16 only requires antibody to a spore *or* vegetative cell of any one of *Bacillus anthracis, B.thuringiensis* or *B.cereus* and is therefore anticipated by the reference.

Claim Rejections - 35 USC § 103

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

12. Claims 16-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kearney et al (WO 99/55842) in view of Loomis et al (WO 99/64863).

Kearney et al teach monoclonal antibodies which are specifically reactive to spores from different species of *Bacillus.* It is taught that the antibodies are highly specific and can discriminate between spores of potentially lethal organisms, such as *B.anthracis,* and other harmless closely related bacilli. See abstract. Figure 6 shows that *anti-Bacillus anthracis* antibody specifically bind *B.anthracis* spores. Example 13, page 18, teaches a monoclonal antibody which specifically reacts with *B.anthracis*, but is not at all reactive with *B.subtilis* or *B.thuringiensis.* Example 14, page 19, teaches a monoclonal antibody which specifically reacts with *B.thuringiensis*, but not *B.subtilis* or *B.anthracis.*

However, Kearney et al does not particularly exemplify the use of a colloidal particle based lateral flow detection system.

Loomis et al teach that colloidal gold particle immunoassays have been successfully used in the prior art for many years. See pages 1-3. Loomis et al teach a more sensitive immunoassay test to what was known in the art. It is a colloidal colorimetric flow through and lateral flow assay. The entire test is conducted on a test strep and the detection antibody is preferably a FAB fragment that has been labeled with a 50-100mm gold particle and immobilized on a test pad. See page 4. It is taught that the use of capture dendrimers to align and secure capture antibodies on a solid surface insure that no immunological activity of the capture antibody is sterically hindered.

It would have been prima facie obvious to one of ordinary skill in the art to use the monoclonal antibodies taught by Kearney in a colloidal lateral flow detection system taught by Loomis et al because Loomis et al teaches that it is a highly sensitive detection assay which is simple, sensitive and specific. The test strips would provide a much more efficient and easy assay then the ELISAs described in Kearney et al. The colloidal lateral flow detection system would have been an obvious modification as it was known in the art as a simple detection system.

13. Claims 17-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mesnage et al (Molec. Microbiol. 1997, 23(6): 1147-1155) in view of Loomis et al (WO 99/64863).

Mesnage et al tach antibodies to the *Bacillus anthracis* S-layer component, EA1. It is disclosed that EA1 constitutes the main lattice of the *B.anthracis* S-layer, and is the major cell-associated antigen. See abstract. Antibodies to the surface array protein (Sap) are also taught. It is taught that a Western blot assay suggested that the antibodies were highly specific to *B.anthracis* and did not cross-react. See page 1150-1151. Electron microscopy using grids with rabbit anti-EA1 antibodies or rabbit anti-Sap antibodies, or on anti-Sap antibodies. The grids were incubated on colloidal gold anti-rabbit or anti-mouse coupled antibodies.

However, Mesnage et al does not particularly exemplify the use of these antibodies in a colloidal particle based lateral flow detection system.

Loomis et al teach that colloidal gold particle immunoassays have been successfully used in the prior art for many years. See pages 1-3. Loomis et al teach a more sensitive immunoassay test to what was known in the art. It is a colloidal colorimetric flow through and lateral flow assay. The entire test is conducted on a test strep and the detection antibody is preferably a FAB fragment that has been labeled with a 50-100mm gold particle and immobilized on a test pad. See page 4. It is taught that the use of capture dendrimers to align and secure capture antibodies on a solid surface insure that no immunological activity of the capture antibody is sterically hindered.

It would have been prima facie obvious to one of ordinary skill in the art to use the antibodies taught by Mesnage et al in a colloidal lateral flow detection system as taught by Loomis et al to detect *B.anthracis* because Mesnage et al teach that the antibodies are highly

specific to *B.anthracis* and that EA1 constitutes the main lattice of the *B.anthracis* S-layer, and is the major cell-associated antigen. One of ordinary skill in the art would have a reasonable expectation that a specific antibody developed against the major cell-associated antigen of a bacterium to be very effective in detecting the bacterium in a sample. Loomis et al teaches that it is a highly sensitive detection assay which is simple, sensitive and specific. The use of the EA1 and/or Sap antibodies taught by Mesange in a colloidal lateral flow detection system would have been obvious as a *B.anthracis* detection system.

14. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15,1989). The Group 1645 Fax number is (703) 308-4242 which is able to receive transmissions 24 hours/day, 7 days/week.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer E. Graser whose telephone number is (703) 308-1742. The examiner can normally be reached on Monday-Friday from 7:00 AM-4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached on (703) 308-3909.

Jennifer Graser
Primary Examiner
Art Unit 1645

6/19/07